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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,655	04/27/2001	Wei Huang	LJL 357	9013

7590 05/19/2003

KOLISCH, HARTWELL, DICKINSON,
McCORMACK & HEUSER
520 S.W. Yamhill Street, Suite 200
Portland, OR 97204

EXAMINER
CHEU, CHANGHWA J

ART UNIT	PAPER NUMBER
1641	16

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

6528323

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Office Action Summary	Application No.	Applicant(s)	
	09/844,655	HUANG ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on th cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *94-115* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *94-115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's canceling claims 1-26 and adding new claims 94-115 has been acknowledged and entered on Page No. 13 on February 27, 2003. Therefore, claims 1-93 are cancelled in this prosecution.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 94-115 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 94, line 4, "contacting the substrate or any product by the operation of the enzyme" is vague and confusing. It is unclear whether applicant in this step contacts the *substrate on*ly, or alternatively it includes the *mixture* of the substrate with the enzyme.

With respect to claim 94, line 4, "contacting the substrate or *any product* by the operation of the enzyme" is vague and confusing. It is unclear what types of enzymatic reaction applicant refers to. Accordingly, it is unclear what the associated products applicant refers to.

With respect to claim 106, line 2, "a macromolecule" is vague and indefinite. It is unclear what "macromolecule" applicant refers to. Specificity of the recited materials needs to be particularly pointing out and distinctly claimed.

With respect to claim 107, line 2, "a nanoparticle" is vague and indefinite. It is unclear what nanometer range of this recited "nanoparticle", albeit "nano" is used but fails the clarification criteria in compliance with 35 U.S.C. §2.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 94-101, 106-108, 110, 112-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov (USP 6472141) in view of Posewits et al. (Anal. Chem. 1999, Vol. 7: 2883-2892).

Nikiforov teaches a fluorescence polarization assay to determine the phosphorylation of a phosphoryatable compound, i.e. phosphotase (dephosphorylate) or kinase (phosphorylate) on the polypeptide substrate. (Col. 3, line 7-20) Nikiforov teaches the steps of conducting the assay includes, first contacting the substrate with the enzyme, then adding a second mixture binding molecule, i.e. proteins (macromolecule) containing metal ion

selected from Fe3+, Ca2+, Ni2+ and Zn2+, and detecting the difference of luminescence polarization emitted from the sample. (supra; Col. 7, line 15-27) Nikiforov teaches that the bound fluorescent molecules show higher fluorescent polarization compared to the unbound molecules, and there is no need of separation of the unbound from the bound molecules for calculation. (supra and the equation (2)) Nikiforov teaches that the product can be flourescently labeled, i.e. luminescent. (claim 18) It is inherent that the phosphorylatable compounds taught by Nikiforov are products of posttranslational modification in the biological system. The binding molecule taught by Nikiforov, e.g. protein, could be viewed as a nanoparticle. Supra. The method taught by Nikiforov also can be applied for screening inhibitors or enhancers of the enzymes. (Col. 7, lines 36-40) Nikiforov also teaches high-throughput, i.e. mass sample array, for the fluorescent polarization method. (Col. 21, line 17-22; Col. 24, line 18-20; Col. 25, line 3-6) However, Nikiforov does not specifically teach using gallium (Ga) metal ion for its fluorescent polarization assay.

Posewitz et al teach using gallium (Ga) rendering more selective and efficient results over the choice of Fe3+, or Al3+ in targeting phospopetides molecule. (See Abstract, and page 2892, Left Col. Second paragraph) Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to replace the conventional metal ions of Fe3+, or Al3+ for capturing phosphopeptides as taught by Nikiforov with the Ga ion as taught by Posewitz et al. with a reasonable expectation of success. The motivation to do so would have been the recognition of the following: (1) Fe3+ and Ga ion have been recognized possessing similar behavior in the ion binding proteins (Posewitz et al. reference, page 2892, Right Column, first paragraph); (2) Ga ion may substitute Fe3+ in study ion binding protein mechanism, supra; (3) Ga ion has been shown more selective and efficient metal ion for targeting phosphopeptides. Supra.

With respect to claim 113, where the recited binding coefficient is no longer than about 10^{-8} M. It would have been obvious to one having ordinary skill in the art at the time the invention was made to optimize the binding assay, since it has been held that where the

general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Allowable Subject Matter

6. Claims 102-05, 109, 111 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

7. The following is a statement of reasons for the indication of allowable subject matter: The closest prior arts taught by Nikiforov and Posewits et al. as discussed supra disclose a fluorescence polarization assay to determine the enzymatic activity of an enzyme operating on a substrate by use of a metal ion, e.g. Gallium. Both Nikiforov and Posewits et al. teach using this method on kinase and phosphotase, but not on phosphodiesterase as recited in this application. Furthermore, the substrate for the phosphodiesterase is nucleotide, which is chemically and biologically distinct from the polypeptides used in both Nikiforov and Posewits' reference. Therefore, prior arts neither teach nor suggest use fluorescence polarization coupling with the Gallium ion to determine the activity of phosphodiesterase.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 703-306-4086. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-3399.

Jacob Cheu
Examiner
Art Unit 1641

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May 15, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
05/17/03